THE POISON PEN

Will There Ever be an Antidote for Drug Shortages?

Erin R. Fox¹ · Kelly Johnson-Arbor^{2,3} · Maryann Mazer-Amirshahi^{3,4}

Received: 31 January 2021 / Revised: 31 January 2021 / Accepted: 8 February 2021 / Published online: 9 March 2021 © American College of Medical Toxicology 2021

Keywords Dimercaprol · BAL · Drug shortages · Lead encephalopathy

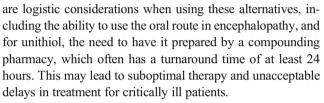
Clinicians familiar with news stories highlighting common drug shortages such as saline solution and anti-hypertensives may be surprised that this persistent public health crisis extends to many common antidotes [1]. Unlike other drug shortages where some product may still be available (albeit a less preferred strength or formulation), antidotes are at a higher risk of significant shortages where no product at all is available. Many antidotes typically do not have a large market share and are generally manufactured by a single company in a single presentation [1]. One such antidote has faced a critical shortage since May 2020 [2]. British Anti-Lewisite (BAL, dimercaprol) is a well-known antidote for the treatment of lead encephalopathy and toxicity from other metals, and it is considered an essential medication by the World Health Organization [3]. According to the American Society of Health-System Pharmacists, BAL has been impacted by 4 discrete shortages since 2006, including the current shortage due to manufacturing problems and regulatory delays [2].

The shortage of BAL has significant implications for patients, particularly those with lead encephalopathy, a lifethreatening condition that requires prompt treatment. Administration of calcium disodium EDTA alone can increase the distribution of lead into the central nervous system and is not recommended. Two alternatives to BAL are succimer and unithiol; however, there are limited data supporting their efficacy in the setting of encephalopathy [4]. Additionally, there

Supervising Editor: Lewis S. Nelson, MD

Maryann Mazer-Amirshahi maryannmazer@gmail.com

- ¹ Department of Pharmacy Services, University of Utah Health, Salt Lake City, UT, USA
- ² National Capital Poison Center, Washington, DC, USA
- ³ MedStar Georgetown University Hospital, Washington, DC, USA
- ⁴ Department of Emergency Medicine, MedStar Washington Hospital Center, Washington, DC, USA



Like many other drug shortages, the shortage of BAL is a result of a lack of resiliency in the supply chain. One point of failure with a single company providing a life-saving product places patients at risk if there is not a plan for redundancy in the system. In the past, the Food and Drug Administration (FDA) has been able to extend the expiration date of available product if the manufacturer can provide stability data; however, in the case of BAL, the manufacturer has no additional details to provide [5]. As such, short-term mitigation strategies are limited. In order to ensure appropriate treatment of poisoned patients, institutions must vigilantly monitor supply and proactively develop protocols to use alternative chelators with the best available, although limited evidence. Outcomes data should be collected when alternative chelators are used to inform treatment protocols. Clinicians should also report cases when BAL is unavailable for a patient to the FDA via MedWatch or on the FDA drug shortage website.

Solutions to the drug shortage problem have been proposed, but few have been enacted. FDA's Drug Shortage Task Force recommends developing a quality rating system to incentivize drug manufacturers to invest in quality facilities as well as promote sustainable contracts to ensure a reliable supply [6]. The CARES Act states that manufacturers must develop risk management and redundancy plans for their supply chains, but this will take time and required actions and accountability are not well defined [7]. Ongoing work by the National Academies of Sciences, Engineering, and Medicine to evaluate the security of the medical product supply chain may also provide solutions [8]. Engagement of industry and balanced incentives are additional potential strategies. While these interventions are taking place in the USA, it is also important to consider that the burden of lead and other heavy



metal toxicity is greater in developing countries where access to antidote is even more limited. Ultimately, a multifaceted approach will be required to ensure that life-saving antidotes such as BAL continue to be available for patients in both the USA and worldwide.

Funding The authors have no financial relationships relevant to this article to disclose.

Declarations

Conflict of interest None.

References

- Mazer-Amirshahi M, Hawley KL, Zocchi M, Fox E, Pines JM, Nelson LS. Drug shortages: implications for medical toxicology. Clin Toxicol (Phila). 2015;53:519–24.
- 2. ASHP Drug Shortages. https://www.ashp.org/Drug-Shortages/ Current-Shortages/Drug-Shortage-Detail.aspx?id= 659&loginretumUrl=SSOCheckOnly. Accessed 30 Jan 2021.

- 3. World Health Organization. WHO model lists of essential medicines. https://www.who.int/groups/expert-committee-on-selection-anduse-of-essential-medicines/essential-medicines-lists. Accessed 26 Jan 2021.
- World Health Organization. Review of succimer for the treatment of lead poisoning. https://www.who.int/selection_medicines/ committees/expert/18/applications/succimer.pdf?ua=1. Accessed 30 Jan 2021.
- U.S. Food and Drug Administration. Search list of extended use dates to assist with drug shortages. https://www.fda.gov/drugs/ drug-shortages/search-list-extended-use-dates-assist-drug-shortages. Accessed 26 Jan 2021.
- FDA Agency Drug Shortage Task Force. https://www.fda.gov/ drugs/drug-shortages/agency-drug-shortages-task-force. Accessed 30 Jan 2021.
- United States Senate. S 3548 Coronavirus Aid, Relief, and Economic Security (CARES) Act. https://www.congress.gov/116/bills/s3548/ BILLS-116s3548is.pdf. Accessed 26 Jan 2021.
- The National Academies of Sciences Engineering and Medicine. Securities of America's Medical Product Supply Chain. https:// www.nationalacademies.org/our-work/security-of-americasmedical-product-supply-chain. Accessed 30 Jan 2021.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.